

A. Amendments to the Specification

The Examiner has objected to the Applicants incorporation of subject matter by reference to a foreign patent (PCT Application WO92/15712) on page 15, line 17 and page 33, lines 25-28 of the specification. Accordingly, Applicants have amended the specification by inserting the relevant sections of PCT Application WO92/15712 into the specification of the presently pending application and eliminated the incorporation by reference in the present application (see MPEP § 608.01(p)). The amendatory material consists of the same material incorporated by reference in the referencing application (see Declaration by Kevin W. McCabe).

The Examiner has also objected to the specification for failing to provide proper antecedent support the definition and substeps of genetic bit analysis. Applicants respectfully submit that the specification, as amended, now provides proper antecedent support for the definition and substeps of genetic bit analysis. Accordingly, the Examiner's objection may be properly withdrawn.

The Examiner has identified several informalities within the specification. Applicants appreciate the Examiner's assistance in this regard and have accordingly amended the specification. Thus, the Examiner's objection may be properly withdrawn.

B. Amendments To The Claims

Applicants have amended claim 30 to clarify that the present invention is drawn to a method for analyzing DNA for the presence of a polymorphic site. Support for the recitation "analyzing DNA for the presence of a polymorphic site" may be found, for example, on page 42, lines 19-21. Likewise, support for the recitation "analyzing DNA of a target human" of claim 31 may be found , for example, on page 42, lines 19-21.

Applicants have amended claims 42 and 45 to clarify that the present invention is drawn to *human* single nucleotide polymorphisms. The recitation "equine polymorphism" is a typographical error. Applicants appreciate the Examiner's assistance in identifying this typographical error. Support for the recitation "human single nucleotide polymorphisms" may be found, for example, on page 58, lines 6-7.

Applicants respectfully submit that no new matter has been introduced by any of the requested amendments.

II. The Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 42-44 under 35 U.S.C. § 112, first paragraph out of a concern that these claims contain subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The recitation "equine polymorphism" in claim 42, line 4 is a typographical error. The claim has been properly amended such that it is presently drawn to a human polymorphism. Accordingly, the Examiner's rejection under 35 U.S.C. § 112, first paragraph may be properly withdrawn.

III. The Rejection of Claims 33, 34, 37 And 40-42 Under 35 U.S.C. § 112, Second Paragraph

Claims 33, 34, 37 and 40-42 have been rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse the Examiner's rejection and request reconsideration.

The Examiner has rejected claims 33 and 34 out of a concern that the limitation "said interrogated single nucleotide polymorphism" lacks sufficient antecedent basis. Applicant respectfully submits that sufficient antecedent basis for the limitation is provided by the limitation "interrogating the single nucleotide polymorphism" found in claim 31, line 14. As there is proper antecedent basis for the limitation "said interrogated single nucleotide polymorphism," the Examiner's rejection may be properly withdrawn.

The Examiner has rejected claim 37 out of a concern that the limitation "said trait" on line 3 lacks sufficient antecedent basis. However, antecedent support for the phrase "said trait" is provided by the phrase "a trait" on line 1 of claim 37. Furthermore, the specification clearly defines the term "trait" to encompass a genetic disease, a condition or a characteristic (see, page 37, lines 28-30). The specification further defines the terms genetic disease, condition and characteristic on page 37, line 30 through page 38, line 2. Accordingly, Applicants respectfully submit that there is proper antecedent support for the limitation "said trait".

Claims 40 and 41 have been canceled. As these claims are no longer pending, the Examiner's rejection that these claims are indefinite may be properly withdrawn.

The Examiner has rejected claim 42 out of a concern that there is insufficient antecedent basis for the limitation "said particular trait". In view of the Examiner's

suggestion and in the interest of furthering prosecution, the Applicants have amended the limitation of claim 42 to "said trait". Applicants respectfully submit, as explained above, that there is proper antecedent support for the recitation "said trait".

The Examiner has further rejected claim 42 out of a concern that the term "using" as found in the phrase "using said determination step" is indefinite. In view of the Examiner's suggestion and in the interest of furthering prosecution, the Applicants have clarified the phrase "using said determination of substep (ii) to determine" to "determining". It is respectfully submitted that the term "determining" as used in claim 42 is not indefinite.

Applicants respectfully submit that the Examiner may properly withdraw the rejection to claims 40 and 41 under 35 U.S.C. § 112, fourth paragraph. As claims 40 and 41 have been canceled, they no longer fail to further limit a preceding claim.

IV. The Rejection of Claims 30 and 32 Under 35 U.S.C. § 102

The Examiner has rejected claims 30 and 32 as being anticipated by Goelet *et al.* under 35 U.S.C § 102(b). Applicants respectfully traverse the Examiner's rejection and request reconsideration.

Applicants respectfully draw the Examiner's attention to the fact that the claimed invention concerns a method for analyzing DNA for the presence of a particular, and defined, polymorphic site - a single nucleotide polymorphism. Claims 30 and 32 have been amended to more clearly describe the invention.

Although the cited Goelet *et al.* publication describes the general use of genetic bit analysis to determine the identity of a nucleotide in a target molecule, it does not appear to disclose to those of ordinary skill the use of genetic bit analysis to analyze DNA for the particular class of polymorphisms - single nucleotide polymorphisms - of concern to the present invention. Since the cited Goelet *et al.* publication fails to disclose an element of the present claims, it cannot anticipate those claims. Accordingly, it is respectfully submitted that the rejection may be properly withdrawn.

V. The Rejection of Claims 31, 33-38, 40, 41, and 45-46 35 U.S.C. § 103(a)

The Examiner has rejected claims 31, 33-38, 40, 41, and 45-46 under 30 U.S.C. § 103(a) as being unpatentable over Goelet, *et al.* It is respectfully submitted that Goelet, *et al.* describes a general method for determining the identity of a nucleotide base at a specific position in a nucleic acid of interest (page 10, lines 33-35). In contrast, the present invention describes the use of that method to analyze DNA for a particular class

of polymorphisms – single nucleotide polymorphisms. Applicants respectfully traverse the Examiner's rejection and request reconsideration.

Although Goelet *et al.* teaches the value of using genetic bit analysis to accomplish microsequencing of DNA, it does not appear to disclose to those of ordinary skill the feasibility (much less the particular advantages) of analyzing single nucleotide polymorphisms.

To this effect, it is respectfully submitted that the cited Goelet *et al.* publication does not disclose that single nucleotide polymorphisms were sufficiently frequent to permit their identification and use in genetic analysis, or that such polymorphisms were sufficiently stable to permit their use in genetic analysis. The advantages of employing single nucleotide polymorphisms are described on page 13, line 20 through page 16, line 23 of the present specification.

In sum, it is respectfully submitted that the cited Goelet *et al.* publication would have provided no motivation for those of ordinary skill to seek single nucleotide polymorphisms, and to use such polymorphisms for genetic analysis.


To this effect, the Examiner proffers that the statement "[m]any techniques have been developed (1) to determine the presence of specific nucleic acid sequences, and (2) to compare homologous segments of nucleic acid sequence to determine if the segments are identical or if they differ at one or more nucleotides" meets the limitation of identifying a "polymorphic site". However, the Goelet, *et al.* reference fails to disclose the use of such methods with respect to the *single nucleotide* polymorphic sites recited in the claims.

Likewise, the Examiner proffers that "[t]he aspect of using primers that specifically hybridize to [the] target nucleic acid speaks to there being an isolation and sequence determination of the target nucleic acid such that primers can be developed and used." However, the Goelet, *et al.* reference fails to teach the use of such methods for identifying the nucleotide present at a *single nucleotide* polymorphic site, as recited in the claims.

Accordingly, it is respectfully submitted that the claimed invention is not obvious in view of the Goelet *et al.* publication, and that the rejection may be properly withdrawn.

Respectfully submitted,

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